



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/728,486	12/05/2003	David J. Ecker	DIBIS-0012US.P1	9735

58057 7590 05/11/2007
MEDLEN & CARROLL LLP
101 HOWARD STREET
SUITE 350
SAN FRANCISCO, CA 94105

EXAMINER

FREDMAN, JEFFREY NORMAN

ART UNIT	PAPER NUMBER
----------	--------------

1637

MAIL DATE	DELIVERY MODE
-----------	---------------

05/11/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/728,486

Applicant(s)

ECKER ET AL.

Examiner

Jeffrey Fredman

Art Unit

1637

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on March 27, 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 27-29,31-35,37,38,50-60,62-71,73-78 and 80-87 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 27-29,31-35,37,38,50-60,62-71,73-78 and 80-87 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on March 27, 2007 has been entered.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Art Unit: 1637

3. Claims 27, 28, 32-34, 36-38, 50, 69, 70, 73-76, 80, 81, 84 and 85 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hurst et al (Rapid Comm. Mass Spectrom. (1996) 10:377-382) in view of either Muddiman et al (Anal. Chem. (1997) 69:1543-1549) or Chen (U.S. Patent 6,613,509).

Hurst teaches a method of claims 27, 69 and 75 of identifying a pathogenic bioagent in sample (see page 377, column 1), comprising:

(a) amplifying a plurality of segments of nucleic acid of said pathogen with a plurality of primer pairs to obtain a plurality of amplification products (see page 378, table I, and page 378, column 2, where PCR was performed using two sets of primer pairs, one directed to the 5S rRNA gene and one directed to the mip gene fragment)

(b) determining the base compositions of at least two members of said plurality of amplification products wherein said base compositions identify said pathogen in said sample (see page 379, figure 1, where Hurst performs MALDI-TOF on both PCR products to determine base composition as the mass of the PCR product, and shows that this is a feasible method of detecting Legionella).

With regard to claims 28, 70, 81, Hurst teaches detection of a bacterial pathogen (see page 379, figure 1, where Legionella is detected).

With regard to claims 32-34, 76, Hurst teaches the use of specific primers that are genus and species specific (see page 378, table 1).

With regard to claim 36, Hurst teaches the base compositions of both the mip and 5S rRNA pcr products (see page 379, figure 1).

With regard to claims 37, 72, 73, 79, 80, Hurst teaches the use of MALDI-TOF (see abstract).

With regard to claims 38, 74, 84, Hurst teaches analysis of the 5S rRNA gene using primers directed to that gene (see page 378, table 1).

With regard to claims 50, 85, Hurst teaches analysis of the mip gene, which encodes a protein involved in virulence (see page 378, table 1).

Hurst does not determine the base composition by identifying the number of individual nucleotides in the amplification product.

Muddiman teaches analysis of base composition of PCR products of microorganisms wherein the base compositions identify the number of each individual nucleotide present in the amplification products without sequencing the amplification products and wherein the base compositions identify the organism in the sample (see abstract). Muddiman exemplifies the base composition analysis in Table 1, showing the base compositions for a variety of PCR products.

Chen also teaches analysis of base composition of PCR products of microorganisms wherein the base compositions identify the number of each individual nucleotide present in the amplification products without sequencing the amplification products and wherein the base compositions identify the organism in the sample (see claim 1, for example).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use the Mass spectrometry base composition analysis methods of Muddiman or Chen in the mass spectrometry analysis method of Hurst since Hurst expressly teaches mass spectrometric analysis of PCR products and since Muddiman expressly teaches "In this work, we have demonstrated that the complementary nature of DNA due to Watson-Crick base-pairing provides constraints that can be exploited in conjunction with the measured mass to allow determination of the number of base pairs and the base composition for relatively large DNA fragments. This approach uses accurate mass measurements and can be extended by the use of mass shifts induced by modified base PCR or postamplification modification, providing a rapid and accurate scheme by which to characterize PCR products of increasing size. This scheme should be particularly attractive for rapid confirmation of the base composition of PCR products (see page 1549, column 2)." An ordinary practitioner would have been motivated to improve the Hurst method by the use of the base composition analysis method of Muddiman in order to rapidly and accurately characterize the PCR products of Hurst down to the base composition level in order to confirm what sequence is present in the sample.

Further and distinct motivation to determine the base composition is provided by Chen, who notes "Using this technique, base compositions of DNA fragments have been determined with an accuracy of $\pm 0.03\%$ with respect to their known sequences. The comparisons of base compositions among homologous sequences are useful in

Art Unit: 1637

sequence validation, sequence comparison, and characterizations of sequence polymorphisms. In particular, the efficiency and accuracy of MALDI-TOF MS which provides analysis of molecular masses of short DNA molecules within seconds are employed to obtain the base composition of a polymerase chain reaction (PCR) product solely from its molecular weight (see column 4, lines 45-56)." An ordinary practitioner would have been motivated to use the Chen method to determine the base composition in order to permit sequence comparisons in an efficient and accurate way using the mass spectrometric method of Hurst combined with the mass spectrometric and analysis methods of Chen.

Therefore, an ordinary practitioner, motivated to detect pathogens by Hurst, would have been motivated by both Muddiman and Chen to perform base composition analysis in order to obtain the benefits of increased speed, accuracy without the requirement to use gel electrophoresis or other sequencing methods.

4. Claims 27-29, 31-35, 37, 38, 50-60, 62-71, 73-78 and 80-87 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hoffman et al (Arch. Virol. (2001) 146:2275-2289) in view of Koster (WO 98/20166) and further in view of either Muddiman et al (Anal. Chem. (1997) 69:1543-1549) or Chen (U.S. Patent 6,613,509).

Hoffman teaches a method of claims 27, 53, 69 and 75 of identifying a pathogenic bioagent in sample (see page 2278, where influenza is the bioagent), comprising:

(a) amplifying a plurality of segments of nucleic acid of said pathogen with a plurality of primer pairs to obtain a plurality of amplification products (see page 2278, subheading "Design of oligonucleotides for RT-PCR" and pages 2278-2281, which detail a PCR reaction that was performed using eight sets of primer pairs, directed to the eight segments of the influenza virus)

(b) determining the base compositions of at least two members of said plurality of amplification products wherein said base compositions identify said pathogen in said sample (see page 2281, figure 3, where the base composition in terms of mass is determined by gel electrophoresis).

With regard to claims 28, 54, 70, 81, Hoffman teaches detection of a viral pathogen (see page 2281, figure 3, where Influenza virus is detected).

With regard to claims 29, 55, 71, 82, Hoffman teaches the use of tissue sample (see page 2277, where tissue from embryonated eggs is used and see page 2276, where virus isolation occurs from the throat of mammals).

With regard to claim 31, 56, 57, 83, Hoffman teaches that samples can be obtained from mammals and teaches the virus infects humans (see page 2276).

With regard to claims 32-34, 58-59, 76, Hoffman teaches the use of specific primers that are viral genus specific (see page 2278).

With regard to claim 35, 60, 77, 78, Hoffman teaches detection of viral subtypes using the primers (see figure 4, page 2282 and figure 5, page 2283 (and table 3) where primers specific for each subtype were used).

With regard to claims 38, 63, 74, 84, Hoffman teaches analysis of all of the genes of Influenza A, including any housekeeping genes (see page 2281, figure 2, where all of the eight segments of Influenza A are amplified).

With regard to claims 50, 51, 64, 65, 85, 86, Hoffman teaches analysis of all of the influenza A virus genes, including genes involved in virulence and the Influenza polymerase genes, PB1, PB2 and PA which form a heterotrimer (see page 2281, figure 2).

With regard to claim 66, 68, Hoffman teaches the use of eight primer pairs (see page 2281, figure 2).

With regard to claim 52, 67, 87, Hoffman teaches analysis "In pandemic situations where a new virus subtype emerges, we could either use the plasmid collection already available or quickly generate plasmids with the same or similar sequences, and use it to develop antiviral therapies (i.e., vaccines). Thus, a universal primer set is a powerful tool that can be used in classic and reverse genetics methods to prevent and contain future influenza A epidemics and pandemics (see page 2287)."

Hoffman teaches PCR to analyze and compare the viral subtypes but does not teach mass spectrometry or base composition signatures.

Koster teaches a method for detecting a single nucleotide polymorphism in an individual using molecular mass measurements such as MALDI TOF (page 14, for example), by determining the molecular mass of said amplification product using mass

spectroscopy (page 13, line 1 and page 157, lines 10-29 and example 19) and comparing the molecular mass to the molecular mass of said region in an individual known to have said polymorphism, where if said molecular masses are the same then said individual has said polymorphism (page 13, lines 2-5 and page 158, lines 1-29, where Koster expressly compares patient 1 to a negative control and example 19).

With regard to claims 36, 37, 61, 62, 72, 73, 79 and 80, Koster expressly teaches comparison of base compositions with both modified and unmodified products wherein the base compositions identify the number of each individual nucleotide present in the amplification products without sequencing the amplification products and wherein the base compositions identify the organism in the sample (see page 66, for example, as well as page 105, table II and pages 69-70). At page 105, table II, Koster provides the base composition of three different PCR products determined by MALDI-TOF. Further, Koster specifically discusses using base composition to analyze mutations as discussed on page 70, where Koster notes "MS can also be used to determined full or partial sequences of larger DNAs; this can be used to detect, locate, and identify new mutations in a given gene region."

In particular, Koster expressly teaches the use of MALDI-TOF for diagnosis of bacterial or viral infections (see pages 73-79). Koster exemplifies this analysis in Example 5.

Muddiman teaches analysis of base composition of PCR products of microorganisms wherein the base compositions identify the number of each individual nucleotide present in the amplification products without sequencing the amplification products and wherein the base compositions identify the organism in the sample (see abstract). Muddiman exemplifies the base composition analysis in Table 1, showing the base compositions for a variety of PCR products.

Chen also teaches analysis of base composition of PCR products of microorganisms wherein the base compositions identify the number of each individual nucleotide present in the amplification products without sequencing the amplification products and wherein the base compositions identify the organism in the sample (see claim 1, for example).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to utilize the Mass spectrometry and base composition analysis method of Koster in the analytical method of Hoffman since Koster states "In another embodiment, an accurate sequence determination of a relatively large target nucleic acid, can be obtained by generating specifically terminated fragments from the target nucleic acid, determining the mass of each fragment by mass spectrometry and ordering the fragments to determine the sequence of the larger target nucleic acid (see page 75, line 26 to page 76, line 2)." So an ordinary practitioner would have been motivated to detect the PCR products of Muddiman with the base composition Mass

Art Unit: 1637

spectrometric approach of Koster since Koster teaches that Mass Spectrometry is accurate and can improve the speed, mass accuracy and precision of the analysis (see abstract, for example).

Further, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use the Mass spectrometry base composition analysis methods of Muddiman or Chen in the mass spectrometry analysis method of Hoffman since Muddiman expressly teaches "In this work, we have demonstrated that the complementary nature of DNA due to Watson-Crick base-pairing provides constraints that can be exploited in conjunction with the measured mass to allow determination of the number of base pairs and the base composition for relatively large DNA fragments. This approach uses accurate mass measurements and can be extended by the use of mass shifts induced by modified base PCR or postamplification modification, providing a rapid and accurate scheme by which to characterize PCR products of increasing size. This scheme should be particularly attractive for rapid confirmation of the base composition of PCR products (see page 1549, column 2)." An ordinary practitioner would have been motivated to improve the Hoffman method by the use of the base composition analysis method of Muddiman in order to rapidly and accurately characterize the PCR products of Hoffman down to the base composition level in order to confirm what sequence is present in the sample.

Further and distinct motivation to determine the base composition is provided by Chen, who notes "Using this technique, base compositions of DNA fragments have been determined with an accuracy of $\pm 0.03\%$ with respect to their known sequences.

Art Unit: 1637

The comparisons of base compositions among homologous sequences are useful in sequence validation, sequence comparison, and characterizations of sequence polymorphisms. In particular, the efficiency and accuracy of MALDI-TOF MS which provides analysis of molecular masses of short DNA molecules within seconds are employed to obtain the base composition of a polymerase chain reaction (PCR) product solely from its molecular weight (see column 4, lines 45-56).” An ordinary practitioner would have been motivated to use the Chen method to determine the base composition in order to permit sequence comparisons in an efficient and accurate way using the PCR method of Hoffman combined with the mass spectrometric and analysis methods of Chen for analysis of PCR products.

Therefore, an ordinary practitioner, motivated to detect pathogens by Hoffman, would have been motivated by all of Koster, Muddiman and Chen to perform base composition analysis in order to obtain the benefits of increased speed, accuracy without the requirement to use gel electrophoresis or other sequencing methods.

Double Patenting

5. Claims 27-29, 31-35, 37, 38, 50-60, 62-71, 73-78 and 80-87 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-29 of U.S. Patent No. 7,108,974. Although the conflicting claims are not identical, they are not patentably distinct from each other because the copending application claims represent a species of the current claims in which specific numbers of species are in the database and where specific mass is determined. Therefore, the

Art Unit: 1637

species of claims 59,60,62,63,66,69-76 and 79-94 of copending Application No.

10/156,608 anticipates the current, more generic claims and renders them prima facie obvious.

6. Claims 27-29, 31-35, 37, 38, 50-60, 62-71, 73-78 and 80-87 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 14-19 and 29-38 of copending Application No.

10/660,997. Although the conflicting claims are not identical, they are not patentably distinct from each other because the copending application claims represent a species of the current claims in which specific numbers of species are in the database and where specific mass is determined. Therefore, the species of claims 14-19 and 29-38 of copending Application No. 10/660,997 anticipates the current, more generic claims and renders them prima facie obvious.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

7. Claims 27-29, 31-35, 37, 38, 50-60, 62-71, 73-78 and 80-87 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-10, 14, 17, 28-44 of copending Application No.

10/660,996. Although the conflicting claims are not identical, they are not patentably distinct from each other because the copending application claims represent a species of the current claims in which specific numbers of species are in the database and where specific mass is determined. Therefore, the species of claims 1-10, 14, 17, 28-

44 of copending Application No. 10/660,996 anticipates the current, more generic claims and renders them prima facie obvious.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

8. Claims 27-29, 31-35, 37, 38, 50-60, 62-71, 73-78 and 80-87 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 23-27, 30-34, 44-55 of copending Application No. 10/660,122. Although the conflicting claims are not identical, they are not patentably distinct from each other because the copending application claims represent a species of the current claims in which specific numbers of species are in the database and where specific mass is determined. Therefore, the species of claims 23-27, 30-34, 44-55 of copending Application No. 10/660,122 anticipates the current, more generic claims and renders them prima facie obvious.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

9. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Response to Declaration

10. The Declaration under 37 CFR 1.132 filed October 6, 2006 is insufficient to overcome the rejection of the claims based upon 35 U.S.C. 103 as set forth in the last Office action because:

The Buchsbaum Declaration, which is the same declaration that has been persuasive in several other related cases, is not persuasive in this case because the skepticism evinced in the declaration is drawn to a requirement for broad range priming (see point 2 on page 2 of the declaration, "To my knowledge, no one ever previously proposed or disclosed combining broad range priming of nucleic acid of bioagents") to perform a comparison with a database of targets (see exhibit B, which discusses both Broad range priming as "TIGER's power comes from the use of broad range primers" and "a phylogenetic tree of relatedness can be constructed"). The importance of the database is exemplified in exhibit 3, which notes that the masses "can be correlated with a database that contains information about RNA weights for a given pathogen".

In the related applications which have been allowed, both of these elements referred to in the Declaration have been present. In U.S. Patent 7,108,974 based upon application 10/156,608, claim 1 requires both primers which flank a variable sequence and a database of 19 or more molecular masses. Similarly, in 10/660,996 and

10/660,997, the claims require primers which flank a variable sequence and a comparison to a database of 19 or more molecular masses.

The current claims lack both requirements that were identified by the Declaration as being responsible for the success and the skepticism of the JASON group and which appear in the exhibits. The claims do not require that the primers flank a variable region and there is no requirement for comparison with a database of sequences. Therefore, the declaration is not persuasive since the claim is not commensurate in scope with the basis of the declaration.

Response to Arguments

11. Applicant's arguments filed March 27, 2007 have been fully considered but they are not persuasive.

Applicant argues that there is no motivation to combine the references. Applicant specifically states that there is no motivation to design primers to organisms other than legionella. This is simply incorrect. Hurst concludes his article with "Mass spectrometry, especially MALDI-TOF MS, offers considerable, potential as a detection method for PCR-amplified bacterial DNA. Developments to extend the upper mass limit while decreasing the amount of material required are being pursued, along with improved rapid purification procedures." Hurst unambiguously motivates detection of bacterial DNA, not just Legionella. The absence of a specific teaching of other organisms does not detract from the motivation to detect and analyze other organisms. Muddiman and Chen teach base composition analysis. In response to applicant's arguments against the references individually, one cannot show nonobviousness by

Art Unit: 1637

attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Applicant then relies upon the Buchsbaum declaration. That is not sufficient for the reasons given above.

Applicant then argues this is an "obvious to try" situation. The legal standard for "reasonable expectation of success" is provided by caselaw and is summarized in MPEP 2144.08, which notes "obviousness does not require absolute predictability, only a reasonable expectation of success; i.e. , a reasonable expectation of obtaining similar properties. See , e.g. , *In re O'Farrell* , 853 F.2d 894, 903, 7 USPQ2d 1673, 1681 (Fed. Cir. 1988)." In this factual case, there is express teaching in the prior art of Hurst that PCR amplification and Mass spectrometric detection would function. There is further evidence as shown in Chen and Muddiman that one mode of Mass spectroscopic analysis is base composition analysis. These were not prophetic teachings by Hurst, Chen and Muddiman, but rather working examples on real world samples. This sufficient for a reasonable expectation of success. The MPEP cites *In re O'Farrell*, which notes regarding "obvious to try" at page 1682, that,

"In some cases, what would have been "obvious to try" would have been to vary all parameters or try each of numerous possible choices until one possibly arrived at a successful result, where the prior art gave either no indication of which parameters were critical or no direction as to which of many possible choices is likely to be successful. E.g. , *In re Geiger* , 815 F.2d at 688, 2 USPQ2d at 1278; *Novo Industri A/S v. Travenol Laboratories, Inc. ,* 677 F.2d 1202, 1208, 215 USPQ 412, 417 (7th Cir.

1982); In re Yates , 663 F.2d 1054, 1057, 211 USPQ 1149, 1151 (CCPA 1981); In re Antonie , 559 F.2d at 621, 195 USPQ at 8-9. In others, what was "obvious to try" was to explore a new technology or general approach that seemed to be a promising field of experimentation, where the prior art gave only general guidance as to the particular form of the claimed invention or how to achieve it. In re Dow Chemical Co ., 837 F.2d, 469, 473, 5 USPQ2d 1529, 1532 (Fed. Cir. 1985); Hybritech, Inc. v. Monoclonal Antibodies, Inc ., 802 F.2d 1367, 1380, 231 USPQ 81, 90-91 (Fed. Cir. 1 986), cert. denied , 107 S.Ct. 1606 (1987); In re Tomlinson ; 363 F.2d 928, 931, 150 USPQ 623, 626 (CCPA 1966).

The court in O'Farrell then, affirming the rejection, notes " Neither of these situations applies here." For the instant case, it is clear that neither situations applies here either. This is not a situation where the prior art suggests varying a variety of parameters, since the prior art directly points to the use of base composition analysis in mass spectroscopy of PCR amplified DNA and teaches mass spectroscopic analysis of PCR amplicons derived from pathogenic bacteria. This is also not a situation where only general guidance was given. The prior art of Hurst, Chen and Muddiman provide specific guidance directing the use mass spectroscopy for the analysis of PCR amplicons, including base composition analysis

As noted in the response to the Declaration, the unexpected nature of the results was based upon the "broad range priming" and the database of agents. Neither of these elements is present in the current claims and therefore, neither of these elements can be relied upon to overcome the prior art. In fact, either element alone is taught by the prior art. The declaration points to the combination of these two elements as provided the unexpected result, which is not present in the current claim set. Therefore, the argument of skepticism of experts is not persuasive since the skepticism is not

Art Unit: 1637

directed towards the actual claims of the current application, but rather to a narrower claim set, not currently present.

Applicant then argues that the motivation is not sufficient and cites to In re Lee, 61 USPQ2d 1430 (Fed. Cir. 2002), arguing that the teaching by Koster that mass spectroscopy improves speed, accuracy and precision are not proper motivations to combine. The Federal Circuit has recently provided a detail explanation of the subsidiary requirement for motivation to combine in Dystar v. Patrick Co., 80 USPQ 2d 1641, 1651(Fed. Cir. 2006) noting,

"Indeed, we have repeatedly held that an implicit motivation to combine exists not only when a suggestion may be gleaned from the prior art as a whole, but when the "improvement" is technology-independent and the combination of references results in a product or process that is more desirable, for example because it is stronger, cheaper, cleaner, faster, lighter, smaller, more durable, or more efficient. Because the desire to enhance commercial opportunities by improving a product or process is universal-and even common-sensical-we have held that there exists in these situations a motivation to combine prior art references even absent any hint of suggestion in the references themselves. In such situations, the proper question is whether the ordinary artisan possesses knowledge and skills rendering him capable of combining the prior art references."

The Dystar court clarifies that motivation exists when the improvement results in a more desirable process and the issue then devolves to whether the ordinary artisan possesses the knowledge capable of combining the references. Here, where the ordinary practitioner is a Ph.D. with several years experience, there is no doubt that the ordinary artisan possesses the knowledge and motivation sufficient to use the advantageous method of Koster with the method of Hoffman, Muddiman and Chen. Some of the listed motivations of Dystar, to result in a more efficient, faster and precise assay, are the precise sorts of motivation identified in Dystar.

As before, the references provide a reasonable expectation of success for the reasons given for the previous 103 rejection. Also, the declaration is not persuasive for the reasons already given above.

Therefore, the rejections are maintained.

Conclusion

12. All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).


A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Fredman whose telephone number is (571)272-0742. The examiner can normally be reached on 6:30-3:00.

Art Unit: 1637

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571)272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.


Jeffrey Fredman
Primary Examiner
Art Unit 1637
